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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,182	12/17/2001	Elisabeth Stockert	LUD-5466.7 DIV	3379

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,182	STOCKERT ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-37,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-37,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 32-37, 40-41 are examined in the instant application.

The following are the remaining rejections.

DOUBLE PATENTING

The submission of the terminal disclaimers is acknowledged and entered.

It is noted that US 6,525,177 and not US 6,524,177, is the patent involved with double patenting. The Examiner apologizes for any confusion and inconvenience incurred by the inadvertent typographic error.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Claims 33-35 remain rejected under 35 USC 112, first paragraph, for while being enabled for the full length amino acid sequence encoded by SEQ ID NO:1, wherein said amino acid sequence is processed by a cell to form a peptide, which complexes to an MHC molecule and is recognized by specific CTLs, but **not enabled for an immunoreactive portion of a protein encoded by SEQ ID NO:1, wherein said immunoreactive portion is processed by a cell to form a peptide which complexes to an MHC molecule and provides a T cell response**, for reasons already of record in paper of 04/23/04.

Claim 41 is rejected under 35 USC 112, first paragraph,for while being enabled for the full length amino acid sequence encoded by SEQ ID NO:1, wherein said amino acid sequence is processed by a cell to form a peptide, which complexes to an MHC molecule and is recognized by specific CTLs, but **not enabled for SEQ ID NO: 4, 5 or 6**, for reasons already of record in paper of 04/23/04.

Applicant argues that there are only two ways a peptide can provoke an immune response, i.e. be an immunoreactive portion of a protein, and it is required that the molecules bind to either class I or a class II MHC molecule. Applicant argues the molecules are presented on T cells and are large enough to generate antibodies. Applicant argues that if the Examiner doubts enablement for, e.g. SEQ ID NO:4, 5, and 6, why does claim 41 not stand as included in the rejection of claim 33-35.

Concerning the Examiner questioning of the statement that SEQ ID NO:4, 5, and 6 are strong stimulators of CTLs, Applicant recites Example 12, pages 24-25, which sets out the experiment, which explains exactly how this was determined. Applicant argues that the Examples in the specification must be accepted as true, unless a factual basis is given for the challenge. Applicant argues that while the Examiner has cited references, none have been applied to Example 12.

Applicant's arguments of paper of 05/20/04 have been considered but are found not to be persuasive for the following reasons:

It is noted that both claims 33-35, and 41 are rejected under 112, first paragraph, because claim 41 reads on claims 33-35, in view of the disclosure in the specification that SEQ ID NOs: 4, 5, 6 are strong stimulators of CTLs specific for the polypeptide

encoded by SEQ ID NO:1, but without any data or analysis supporting the disclosure. However, claims 33-35 are rejected separately from claim 41, because although both the immunoreactive portions of claims 33-35, and SEQ ID NO:4, 5, 6 are not enabled for being processed by a cell to form a peptide, which complexes to an MHC molecule and provides a T cell response, claims 33-35 encompass any portion of the polypeptide encoded by SEQ ID NO:1, of any structure, whereas claim 41 encompasses a specific peptide, i.e. SEQ ID NO: 4, 5 or 6.

Concerning claims 33-35, the claims require that the peptide molecules bind to either class I or a class II MHC molecule, and provide any T cell response, such as inducing specific CTLs, wherein said peptides are of undisclosed structure, provided said peptides is part of the polypeptide encoded by SEQ ID NO:1. Applicant has not taught the structure of the claimed peptides from the polypeptide encoded by SEQ ID NO:1 that meet the required properties. In other words, Applicant has not taught how to make such claimed peptides, in view that not any peptide of a polypeptide could bind to HLA, as taught by Roitt et al, and Stites et al, all of record, and that not any of those peptides that potentially could bind to HLA could induce any T cell response, such as inducing specific CTLs, as disclosed by Kirkin et al, of record, and it would be undue experimentation for one of skill in the art to screen such peptides that could induce any T cell response.

Concerning claim 41, it is not clear on what basis that the statement of Example 12 that SEQ ID NO: 4, 5, 6 are the best stimulators of CTLs was made, especially in view of the teaching of Kirkin et al, of record, that only few peptides from melanoma

associated antigens have been so far identified as being recognized by specific CTLs, and it is unpredictable that not any peptide would be recognized by CTLs. Although methods for screening peptides that are recognized by CTLs are disclosed in the specification, and are routine in the art, however, in view of the above teaching in the art and in the absence of objective evidence, it is not possible to determine that SEQ ID NO:4, 5, and 6 have the property of providing a T cell response to the full length parent protein, and thus one would not know how to use the claimed SEQ ID NO: 4, 5 or 6.

2. Claims 33-35 remain rejected under 35 USC 112, first paragraph, because the specification while being enabled for the full length amino acid sequence encoded by SEQ ID NO:1, wherein said amino acid sequence is processed by a cell to form a peptide, which complexes to an MHC molecule and is recognized by specific CTLs, but not enabled for an immunoreactive portion of a protein encoded by SEQ ID NO:1, wherein said immunoreactive portion is processed by a cell to form a peptide which complexes to an MHC molecule and provides a T cell response **in vivo**, as contemplated, for reasons already of record in paper of 04/23/04.

Applicant argues that the Examiner rejects a claim that is not presented, and that claims 33-35 do not recite providing a T cell response in vivo.

Applicant's arguments of paper of 05/20/04 have been considered but are found not to be persuasive for the following reasons:

Although the claims 33-35 do not recite providing a T cell response in vivo, however, in view of the contemplation of administrating to a patient peptides of the protein encoded by SEQ ID NO:1, that provokes lysis of target cells for immunotherapy

in the specification, claims 33-35 encompasses an immunoreactive portion of a protein encoded by SEQ ID NO:1, wherein said immunoreactive portion is processed by a cell to form a peptide which complexes to an MHC molecule and provides any T cell response **in vivo, as contemplated.**

REJECTION UNDER 35 USC 102(b or e), NEW REJECTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 32, 40 are rejected under 35 U.S.C. 102(b or e) as being anticipated by Morgan DG et al, 1995, J Mass Spectrometry, 30(3): 473-477.

Claims 32 and 40 are drawn to an isolated protein consisting of an immunoreactive portion of a protein encoded by an isolated nucleic acid molecule, consisting of the nucleotide sequence of SEQ ID NO:1. Said immunoreactive portion of the protein is an amino acid sequence of a tumor rejection antigen.

Morgan DG et al teach a tripeptide Gly-Gly-XXX where XXX is Pro.

It is noted that Gly-Gly-Pro is exactly the same as the amino acids 32-34 of the amino acid sequence encoded by SEQ ID NO:1, as shown in the sequence listing on page 36.

It is further noted that there is no definition of immunoreactive portion in the specification.

The peptide taught by the art seems to be the same as the claimed protein.

Although the references do not specifically teach an immunoreactive portion of a protein encoded by SEQ ID NO:1, wherein the protein is an amino acid sequence of a tumor rejection antigen, however, the claimed immunoreactive portion appears to be the same as the prior art peptide. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the

applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

REJECTION UNDER 35 USC 103, NEW REJECTION

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan DG et al, 1995, J Mass Spectrometry, 30(3): 473-477, in view of Rankin EM, 1993, Diagnostic Oncology, 3(5): 280-286, and Jones, T et al, 1994, Eur J Clin Microbiol & Infectious diseases, 13, Suppl 2; S47-53.

Claims 36-37 are drawn to the isolated protein of claim 32 and an adjuvant, wherein said adjuvant is a saponin, GM-CSF or an interleukin.

The teaching of Morgan DG et al has been set forth above.

Morgan DG et al do not teach an adjuvant, wherein said adjuvant is a saponin, GM-CSF or an interleukin.

Rankin EM teaches that adjuvants such as interleukin-2 or GM-CSF stimulate the immune response.

Jones et al teach injection of GM-CSF as an adjuvant increases antibody titers to foreign antigens.

Therefore, it would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to formulate the peptide taught by Morgan DG et al with an adjuvant, such as GM-CSF or an interleukin, as taught by Rankin or Jones et al, because adjuvants increase the immune response, as taught by Morgan DG et al, or US 5106834.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS
July 22, 2004

SUSAN UNGAR, PH.D
PRIMARY EXAMINER